ISSN 2278–540X EISSN 2278–5396

DRUG DISCOVERY

Lantana camara ameliorates gastric ulcer in aspirin-induced ulcer in wistar rats

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Article History
Received: 25 January 2020
Accepted: 04 March 2020
Published: March 2020

Citation
Gabriel D. Edem, Sarah I. Essien, Akpan U. Ekanem, Kingsley A. Okon, Samuel S. Gabriel. *Lantana camara* ameliorates gastric ulcer in aspirin-induced ulcer in wistar rats. *Drug Discovery*, 2020, 14(33), 50-56

ABSTRACT

Traditional medicine has been of immense importance to the world teeming populace. A total of (16) sixteen rats were used for this investigation to affirm the traditional use of *Lantana camara* in the treatment of ulcer. They were divided into 4 groups of 4 animals each, the following parameters were measured and recorded, ulcer score, PH, gastric acid and proteins. The plant has been found to reduce ulcer score, reduce PH and reduce gastric acid secretion. This indicated and affirms the anti-ulcer potentials of the widely used plant.

Keywords: ulcer, ulcer score, *Lantana camara*, traditional medicine

1. INTRODUCTION

Plant products have been used for therapeutic purposes over the years. The world Health Organization (WHO) estimated that 80% of people still rely on traditional remedies such as herbs for their medicines [1]. The plants are also sources of many modern medicines. It is estimated that approximately a quarter of processed drug contain plant extracts or active ingredient obtained from or modeled on plant substances [1]. *Lantana camara* is a low and scandent shrub. It can grow up to 1.2-2.4m high with stout recurved prickles and having strong odour of black currents. *Lantana camara* is a flowering ornamental plant belonging to family verbenaceae [2]. Its leaves are opposite, Ovate or Ovate-oblong, acute or subacute and crenate-senerrate. *Lantana camara* is a perennial flowering plants native to tropical regions of the Americans and Africa [3]. The aromatic flowers are borne in clusters and are a mixture of red, yellow, blue, lilac, white and orange floret [4]. Other common names of this plant include shrub verbena, *Lantana* weed, coronitas, yellow sage and tick berry. *Lantana camara* has a variety of local names in Nigeria, they include, Ewonadele in Yoruba, Kimbamahalba in Hausa and Anya nnunu in Igbo [5]. *Lantana camara* is one of the most useful medicinal weeds in the world. *Lantana camara* has many uses, particularly in traditional medicine. The flowers act as Nectar source for butterflies and moths. Stalks of *Lantana camara* are used for wrapping in paper pulp industries [3]. The extract of *Lantana camara* has been used in the treatment of cancer, ulcer, chicken pox, measles, asthma, swelling, eczema, tumors, high blood pressure, tetanus, rheumatism and malaria in folk medicine [6].

It is also used for the treatment of skin itches, as an antiseptic for wounds, and externally for leprosy and scabies [6]. *Lantana camara* leaves have been employed as an antitumoral, antibacterial, antihypertensive agent and espectorant [7]. The funks are useful in fistula, pustules, tumors and rheumatism. Essential oil constituents of *Lantana camara* include sabiene (19.6-21.5%), 1, 8-cineole (12.6-14.8%), β-caryophyllene (12.7-13.4%), humulene epoxide – III and 8-hydroxy bicyclogermacrene, 8-cineol (15.8%), sabinene (4.7%) and caryophylene (8.9%). *Lantana camara* also contain tannin, catachin, saponin, steroids, alkaloids, phenol, anthroquinone, proteins, tri-terpenoids, flavonoids, glycosides and reducing sugars which are mainly responsible for exerting diverse biological activities [7]. Gastric ulcers are breakages in the continuity of the mucosal epithelial lining of the stomach. It can also occur in areas of ectopic gastric tissue and in small and large bowels in Zollinger-Ellison syndrome.

2. MATERIALS AND METHODS

Animals Handling

A total of sixteen (16) male albino Wistar rats weighing between 170-200g were procured from University of Uyo, College of Health Science animal House for the experiment. Before the commencement of the experiment, the animals were examined and weighed. The rats were housed in wooden cages with adequate space to enhance free movement and good ventilation. Saw dust was used as bedding inside the cage and were replaced with clean ones every two days. They were allowed twelve hours light and twelve hours dark cycle at the normal room temperature obtainable in the test environment and fed on a standard rat diet (Vital Feed Growers, Green Cereals Nigeria Ltd) and water *ad libitum*. Rats were kept for two weeks for acclimatization and were handled from time to time to minimize the stress during the experiment. The animals were divided into four groups (A, B, C and D) with 4 animals in each group.

Drug Preparation

Aspirin (acetylsalicylic acid) was prepared by dissolving 300mg in 10 ml of distilled water. Omeprazole was prepared by dissolving a single tablet (20mg) in 10ml of distilled water and administered to the animal for 14 days.

Plant Collection and Identification

Lantana camera was obtained from Ekom Iman along Etinan-Uyo highway, Akwa Ibom State and identified at the Department of Botany and Ecological studies, University Of Uyo with the Herbarium number: UUH 4023(Etinan).

Plant Extraction

After identification, the leaves of *Lantana camara* were taken to the Department of Biochemistry, Faculty of Basic Medical Sciences, University of Uyo. The leaves were air dried, cut into pieces and pulverized to powder. The powdered *Lantana camara* leaves were weighed and macerated in ethanol for 72 hours. At the end of 72 hours, it was filtered, and the filtrate was concentrated to dryness in a water bath at 45°C.

Experimental Protocol

Before the start of administration, the animals were acclimatized for two weeks. All animals were divided into four groups (A, B, C and D) with 4 animals in each group (n=4). Group A received distilled water for 14 days, Group B was administered with 300mg/kg b.wt of aspirin intraperitoneally (single dose) after 36 hours of starvation. Group C received 300mg/kg b.wt of aspirin intraperitoneally plus ethanolic extract of 250mg/kg *Lantana camara* orally, 6 hours after aspirin induction for 14 days. Group D received 300mg/kg b.w of aspirin intraperitoneally plus 20mg/kg b.wt of omeprazole given daily for 14 days.

Induction of Ulcer

During the entire experimental period, the animals were examined and their weight checked before commencement of administration of aspirin, *Lantana camara* extract and Omeprazole. Before sacrifice, the weights of the animals were taken again to determine the final weight. After the 36 hours starvation, the animals were weighed and maintained in their individual cages with the administration of water only. 300mg/kg of Aspirin was injected intraperitoneally and the animals were deprived from both food and water for 6 hours. One animal from group B was sacrifice after 6hours of administration to check for ulceration which shows that all the animal in group B, C, D had develop ulcer. After 14 days of administration, the animals were anaesthesized by chloroform inhalation and sacrificed. The abdomen were cut open and the stomach of the animals of each group was excised through the greater curvature with the oesophagus closed. The gastric contents were collected into the centrifuge tubes to check for gastric volume, protein, pH and acidic level after which the stomachs were flushed with normal saline and then stretch on a wooden board to check for ulcer using X10 lens.

Measurement of Ulcer Index

Stomach mucosa was flushed with saline and lesions in glandular portion were then exposed and examined under a X10 magnifying glass. Ulcer index of each animal was calculated by the addition of the values and their mean values. The percentage preventive index was calculated according to the method of Hano et al. (1976), which is expressed as:

$$\text{Preventive Index (\%)} = \frac{\text{(U.I Aspirin – U.I Extract/drug plus) Aspirin} \times 100}{\text{U.I (Aspirin)}}$$

Where U.I = ulcer index

Collection of Gastric Content

The stomachs of aspirin induced ulcer in rats were carefully excised. The oesophagus was kept closed, the greater curvature was opened and the luminal contents were removed. The gastric content thus collected was centrifuged at 3000 rpm for 10 minute and expressed in terms of ml/100g of body weight.

Test for protein

The method of Kjeldahl (1883)[8] was used for this test. 1g of the sample was thoroughly weighed into a standard 250ml Kjeldahl flask which contains 1.5g $CuSo_4$ and 1.5g of $NaSo_4$ as catalyst and 5ml concentrated H_2SO_4. Kjeldahl flask (digestion) was placed on a heating mantle and was heated gently to prevent frothing for some hours until a clear bluish solution was obtained. The digestion solution was allowed to cool and this was quantitatively transferred to 100ml standard flask and make up to the mark with distilled water. 20ml portion of the digestion was dropped into a semi micro Kjeldahl distillation apparatus and mixed with similar volume of about 40% of NaOH solution. Ammonia evolved was stream- distilled into a 100ml conical flask containing 10ml solution of saturate boric acid to which 2 drops of Tashirus indicator (double indicator) was added. About 2/3 of the original volume was obtained by immersing the tip of the condenser into boric acid double indicator solution. The tip of the condenser was rinsed with a few millimeters of distilled water in the distillate which was titrated with 0.1M of hydrochloric acid until a purple- pink end point was obtained.

Test for acidity

5g of the gastric sample was added to Erlenmeyer flask and 10ml of distilled water was also added. The flask was heated for about 1 minute to drive off the dissolved carbon dioxide. The Erlenmeyer flask was cooled and 5 drops of phenolphthalein was added and titrated with 0.1M NaOH until a light pink colour was obtained. The measurements were noted for calculation

Formula = $\frac{V \times 0.1 \times 0.6}{\text{Wt of sample taken}} \times 100$

3. RESULTS

Effects of *Lantana camara* on gastric acid secretion in male wistar rats

Gastric acid output was significantly increased ($p<0.05$) in the aspirin induced ulcer group when compared with the control group. Gastric acid output was significantly decreased ($p<0.05$) in the aspirin induced ulcer plus *Lantana camera* extract treated group when compared with the aspirin induced ulcer group. Gastric acid output was also significantly decreased ($p<0.05$) in the aspirin induced ulcer plus omeprazole treated group when compared with the control. Gastric acid output was also significantly decreased ($p<0.05$) in the aspirin induced ulcer plus omeprazole treated group when compared with the aspirin induced ulcer group (fig. 1).

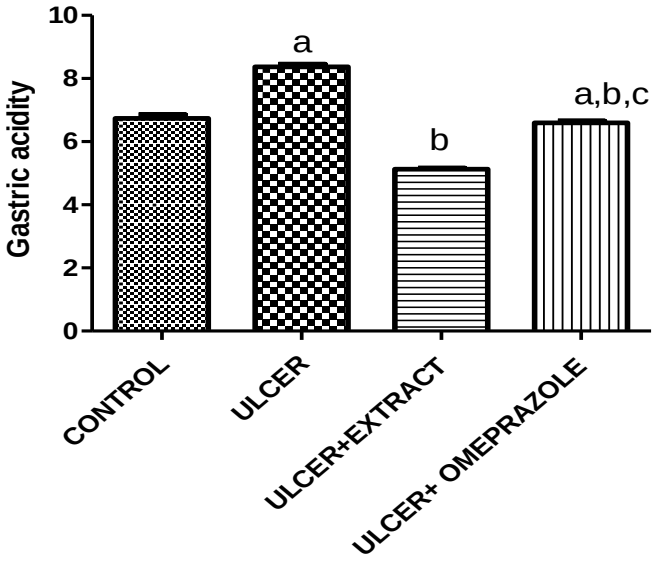

Figure 1 Gastric acid secretion in male wistar rats administered with *Lantana camara*. Columns represent mean ± SEM. n = 3. [a]$p<0.05$ when compared with the control group. [b]$p<0.05$ when compared with aspirin induced ulcer group. [c]$p<0.05$ when compared with aspirin induced ulcer group plus *Lantana camara extract*. Analysis was based on one way analysis of variance (ANOVA) and Tukey post hoc test.

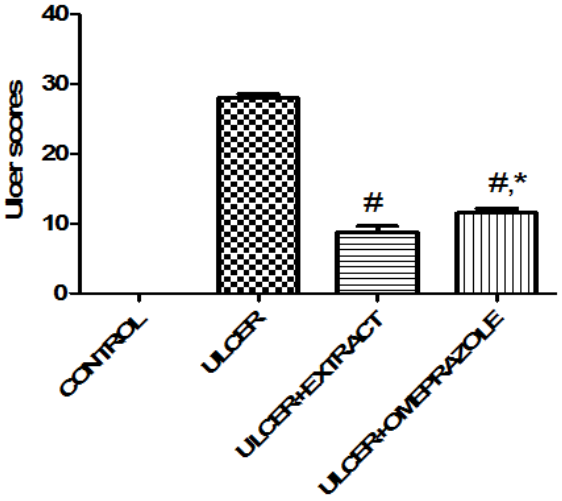

Figure 2 Ulcer scores in male wistar rats administered with *Lantana camara*. Columns represent mean ± SEM. n = 3. [#]$p<0.05$ when compared with aspirin induced ulcer group plus *Lantana camara extract*. Analysis was based on one way analysis of variance (ANOVA) and Tukey post hoc test.

Effects of *Lantana camara* on ulcer scores in male wistar rats

Ulcer score was also significantly decreased ($p<0.05$) in the aspirin induced ulcer plus *Lantana camara* extract group and aspirin induced ulcer plus omeprazole treated group when compared with the aspirin induced ulcer group (figure 2).

Effects of *Lantana camara* on pH in male wistar rats

The pH was significantly increased ($p<0.05$) in the aspirin induced ulcer. pH also significantly decreased ($p<0.05$) in the aspirin induced ulcer plus *Lantana camera* extract treated group when compared with the aspirin induced ulcer group. pH was also significantly decreased ($p<0.05$) in the aspirin induced ulcer plus omeprazole treated group when compared with the aspirin induced ulcer plus *Lantana camera* extract treated group (figure 3).

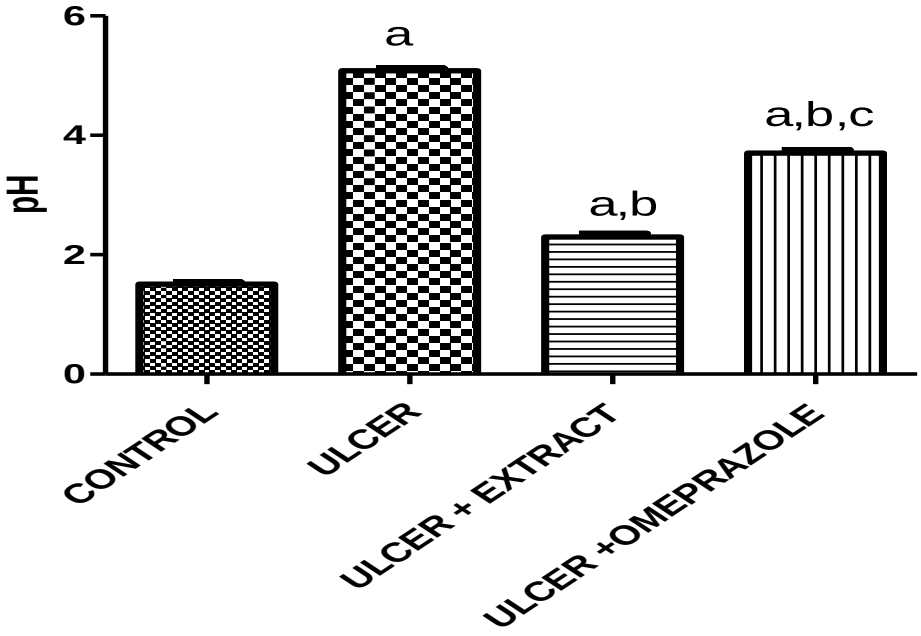

Figure 3 pH in male wistar rats administered with *Lantana camara*. Columns represent mean ± SEM. n = 3. [a]$p<0.05$ when compared with the control group. [b]$p<0.05$ when compared with asprin induced ulcer group. [c]$p<0.05$ when compared with aspirin induced ulcer group plus *Lantana camara extract*. Analysis was based on one way analysis of variance (ANOVA) and Tukey post hoc test.

Effects of *Lantana camara* on total protein levels in male wistar rats

The total protein levels was significantly decreased ($p<0.05$) in the aspirin induced ulcer, aspirin induced ulcer plus *Lantana camera* extract and aspirin induced ulcer plus omeprazole treated groups when compared with the control group. Total protein levels was also significantly increased ($p<0.05$) in the aspirin induced ulcer plus omeprazole treated group when compared with the aspirin induced ulcer, aspirin induced ulcer plus *Lantana camara* extract groups respectively (figure 4).

4. DISCUSSION

The use of plants extract in traditional medicine continues to provide the therapeutic needs for greater percentage of the world's population especially in developing countries [9, 10]. *Lantana camara* plant components have been employed to variety of importance and application in herbal medicine due to the presence of secondary metabolites present in this plant. The use of chemicals from plants has been recognized from ages [11]. The high phytochemical content observed in this plant has made it a unique material for medicinal drug screening and research. The observed protective effect and ability of *Lantana camara* to reduce ulcer index in the extract treated group is an indication of its vasoconstricting effect due to some phytochemicals (tannins) present in the plant. These results compared favourably with the gastric ulcer lowering effects of *Exoecaria aggallocha* [12] and the astringent action of tannins [13]. Free radical scavenging ability of flavonoids has been reported to protect the gastrointestinal tract

from ulcerative and erosion lesion [14]. Also the reduction in the ulcer index of the aspirin plus extract treated group could be due to the antioxidant activity of the plants; this is in agreement with report of [15].

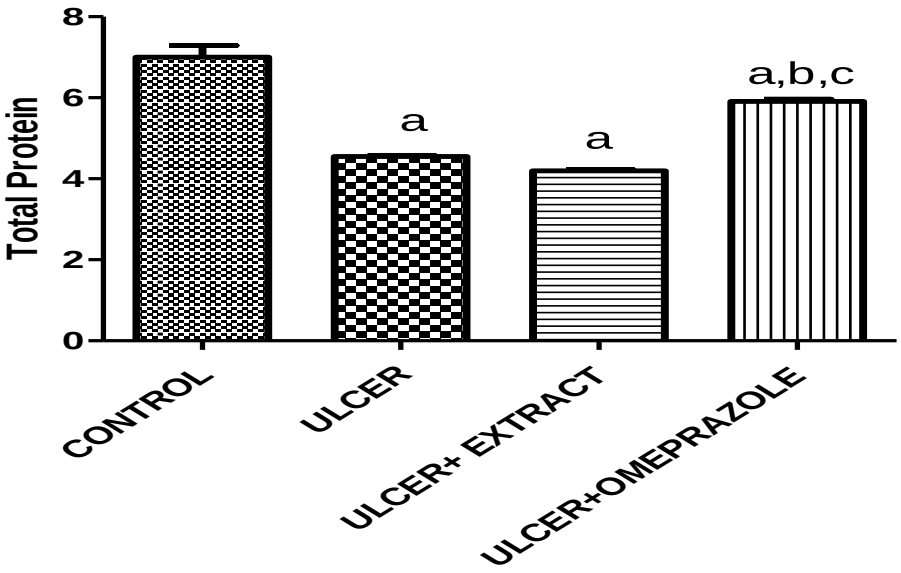

Figure 4 Total proteins in male Wistar rats administered with *Lantana camara*. Columns represent mean ± SEM. n = 3. [a]p<0.05 when compared with the control group. [b]p<0.05 when compared with asprin induced ulcer group. [c]p<0.05 when compared with aspirin induced ulcer group plus *Lantana camara extract*. Analysis was based on one way analysis of variance (ANOVA) and Tukey post hoc test.

The volume of acid present in gastric secretion which encompasses hydrochloric acid, pepsinogen, mucus, bicarbonates, intrinsic factor and protein reflects acid volume. Exposure of unprotected lumen of the stomach to accumulating acid could facilitate ulceration [16]. The content of acid present in gastric juice is another major aggressive factor responsible for ulcer. Over secretion of histamine contributes to increased secretion of gastric juice [17]. When the concentration of hydrogen ions in gastric juice decreases, it is a reflective of high pH. The beginning of ulcer and gastric damage is enhanced by hydrogen ions which is another aggressive factor [18]. Decreased prostaglandin level impairs almost all aspects of gastro protection and increases acid secretions which, in turn, aggravate the ulcer [19]. It is likely that protection by the extract against aspirin-induced gastric ulceration is achieved by the suppression of acid secretion. Similarly, the extract may have blocked histamine-induced contractile responses in a similar fashion as the standard drug, Omeprazole. The anti-histamine effect of the extract could be due to one or several phytochemicals present in the plant extract. Flavonoids have been demonstrated to antagonize the effects of histamine which is a major mediator in ulcerogenesis [20]. The result from this present studies is in line with earlier research by [13] who noted that the ethanol extract of *Buchholzia coriacea* seed was found to reduce the gastric secretion and acidity due to its ability to suppress the effect of histamine which is likely to play a role in the observed activity. The protective effect of the plant extract could also be due to its antisecretory potential and antioxidant activity. The increase in gastric volume of the treated aspirin group is due to increased production of hydrochloric acid as it is evident from the total acidity of the gastric juice. The decrease in the protein content of the gastric mucosa in the ulcerogenic group may be due to damage in the gastric mucosa which results, in the leakage of protein into the gastric juice. Treatment with plant extracts increased the mucosal protein which indicates its ability to enhance cell proliferation and stimulates the growth of the gastric mucosa.

5. CONCLUSION

Lantana camara significantly ameliorates ulcer in male wistar rats by reducing gastric acidity and pH, ulcer score etc.

Funding:
This study has not received any external funding.

Conflict of Interest:
The authors declare that there are no conflicts of interests.

Peer-review:
External peer-review was done through double-blind method.

Data and materials availability:
All data associated with this study are present in the paper.

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